REMARKS

Claims 1-33 are pending in the present application, with claims 16-33 having been withdrawn from consideration. Claims 16-33 have been canceled herein without prejudice to Applicants' pursuing these claims in one or more related applications. Claim 11 has been amended herein; new claims 34 and 35 have been added herein. Thus, upon entry of the present amendment, claims 1-15, 34 and 35 will be under examination.

Regarding the amendments

In the specification:

The specification has been amended to indicate that the present application is a continuation-in-part of U.S. Serial No. 09/560,915. This amendment is supported by the transmittal for filing of the present application on August 17, 2001, which states that this application is a "continuation-in-part under CFR 1.53(b)(2) of prior application serial no. 09/560,915, filed April 28, 2000." A copy of the application transmittal is submitted herewith as Exhibit A. This amendment to the specification merely corrects the priority information and adds no new matter.

In the claims:

Claim 11 has been amended to independent form.

New claim 34 is directed to a method of promoting wakefulness in a mammal involving administering to the mammal an effective amount of a Prolactin-Releasing Peptide (PrRP) or PrRP functional analog. New claim 35 depends from claim 34 and recites administering a PrRP. New claims 34 and 35 are supported throughout the specification, for example, at page 18, lines 21-24, which indicates that exemplary PrRP receptor agonists include PrRP and a PrRP functional analog, and by claim 15 as originally filed.

As set forth above, the amendments and new claims are fully supported by the specification and claims as originally filed and do not introduce new matter. Accordingly, entry of the amendments and new claims is respectfully requested.

Regarding the claim objection

The Office Action states that claims 11 and 12 are objected to as depending upon a rejected base claim. Applicants have herein amended claim 11 to independent form. Claim 12 depends from claim 11. Therefore, these claims are in condition for allowance.

Regarding the rejection under 35 U.S.C. § 112, first paragraph, enablement

The objection to the specification and corresponding rejection of claim 15 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in the specification, are respectfully traversed.

The Office Action acknowledges that the specification is enabling for a method of promoting wakefulness in a mammal that involves administering to the mammal an effective amount of PrRP. Applicants draw the Examiner's attention to new claims 34 and 35, which are directed to subject matter indicated in the Office Action to be enabled by the specification.

The Office Action asserts that the specification lacks enablement for the claimed method when practiced using a PrRP receptor agonist. Specifically, the Office Action states that the claim fails to recite any structural or functional limitations; that the specification lacks guidance regarding which structural features of a PrRP receptor agonist are required to provide activity; and that working examples are absent.

Applicants submit that the specification provides enablement for the full scope of claim 15, for example, by teaching multiple exemplary PrRP receptor agonists that would have been used by those skilled in the art for practicing the claimed method. Exemplary PrRP receptor agonists disclosed in the specification, include, for example, three PrRP-31 amino acid

sequences (page 19, lines 20-24); three PrRP-20 amino acid sequences (page 20, lines 1-6); a seven amino acid PrRP (SEQ ID NO:23). Moreover, using guidance provided in the specification and routine screening methods, a variety of PrRP receptor agonists useful in the claimed method would have been identified by one skilled in the art. For example, the specification provides guidance to those skilled in the art for identifying a PrRP receptor agonist by performing PrRP receptor signaling assays (page 29, line 21, to page 30, line 17; and page 35, line 29, to page 30, line 11) and PrRP receptor binding assays (page 37, lines 9-22). Using this guidance, those skilled in the art would have been able to make and use a variety of PrRP receptor agonists useful in the claimed method.

The Office Action asserts that the specification lacks guidance regarding which structural features of a PrRP receptor agonist are required to provide activity. Applicants submit that the specification teaches structural features of a PrRP receptor agonist required to provide activity, for example, by disclosing that the C-terminus of PrRP is important for activity (page 23, line 28, to page 24, line 5) and that the N-terminus of PrRP is highly tolerant of modifications (page 23, lines 22-27). In addition, the specification discloses multiple exemplary species orthologs of PrRP (see, for example, page 19, lines 20-24, and page 20, lines 1-6), and teaches that an alignment can be performed among PrRP sequences of various species to determine residues and regions in which modification are likely to be tolerated (p-age 23, lines 16-19). In view of this guidance provided in the specification for structural features of a PrRP

agonist important for activity, Applicants submit that those skilled in the art would have been able to make and use a variety of PrRP receptor agonists in the claimed method using only routine methods.

The Office Action asserts that claim 15 fails to recite any structural or functional limitations for the PrRP receptor agonist. Applicants submit that, in contrast to this assertion, the recited PrRP receptor agonist has the functional characteristic of selectively promoting or enhancing normal signal transduction through the PrRP receptor (page 18, lines 11-13). Thus, the specification provides guidance to those skilled in the art by teaching that the claim method is practiced using a compound that selectively promotes or enhances normal signal transduction through the PrRP receptor.

The Office Action asserts that "the specification discloses literature which demonstrates that various PrRP mutants can bind the PrRP receptor and stimulated calcium mobilization, but this is an *in vitro* assay." Applicants respectfully point out that regardless of the assay used to identify a PrRP receptor agonist, the identified agonist would be expected to work in the claimed method. In this regard, the specification teaches that a "PrRP receptor agonist" is a compound that selectively promotes or enhances normal signal transduction through the PrRP receptor (page 18, lines 11-13), and that administering of a PrRP receptor agonist promotes wakefulness in a mammal (see, for example, page 89, lines 18-29). Based on the teachings in the specification of the functional characteristics of a PrRP

receptor agonist, one skilled in the art would have understood that, regardless of the method used for identifying a particular agonist, a PrRP receptor agonist selectively promotes or enhances normal signal transduction through the PrRP receptor whether the receptor is in a test tube or in an animal.

The Office Action asserts that "the specification does not teach or provide working examples of any variant sequence which would be within the claims (having the activity or promoting wakefulness in a mammal)." In contrast to this assertion, Applicants point out that the specification teaches PrRP variants containing substitutions of Ile25, Pro27, Val28, or Phe31 (page 24, lines 8-18). Applicants submit that these and other PrRP variants that retain characteristics of a PrRP receptor agonist would have been made and used by those skilled in the art for use in the claimed method.

The Office Action implies that specification must show working examples for multiple species to prove that a PrRP receptor agonist has the activity recited in the preamble of the claims. Applicants submit that, based on the teaching in the specification that administering PrRP promotes wakefulness in a mammal (page 88, lines 3-29), those skilled in the art would have understood that a variety of PrRP receptor agonists would have been used in the claimed method. In view of this, and of the disclosure in the specification of multiple PrRP receptor agonists (see, for example, page 19, lines 20-24, and page 20, lines 1-6) one skilled in the art would have been able to practice the claimed method without undue experimentation.

In view of the above remarks, Applicants respectfully request that the Examiner reconsider and remove the enablement rejection under the first paragraph of 35 U.S.C. § 112.

Regarding the rejection under 35 U.S.C. § 112, first paragraph, written description

The objection to the specification and corresponding rejection of claim 15 under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient description of the claimed method to reasonably convey to one skilled in the relevant art that the inventors were in possession of the claimed invention at the time the application was filed, are respectfully traversed.

The Office Action acknowledges that the specification provides adequate written description for a method of promoting wakefulness in a mammal that involves administering to the mammal an effective amount of PrRP. Applicants draw the Examiner's attention to new claims 34 and 35, which are directed to subject matter indicated in the Office Action to have sufficient written description in the specification.

Applicants submit that the specification provides written description sufficient to convey to one skilled in the art that Applicants had possession of the invention of claim 15, which is directed to a method for promoting wakefulness in a mammal by administering a PrRP receptor agonist. The specification provides guidance, for example, by disclosing several exemplary PrRP receptor agonists useful in the claimed

method. Such agonists include, for example, three PrRP-31 amino acid sequences (page 19, lines 20-24); three PrRP-20 amino acid sequences (page 20, lines 1-6); and a seven amino acid PrRP (SEQ ID NO:23; page 23, line 28, to page 24, line 5). The specification further teaches the functional attributes of a PrRP receptor agonist. Specifically, the specification teaches that a PrRP receptor agonist selective promotes or enhances normal signal transduction through the PrRP receptor (page 18, lines 11-13). Given the written description of multiple exemplary PrRP receptor agonists and functional attributes of a PrRP receptor agonist disclosed in the specification, it would have been clear to the skilled artisan that Applicants were in possession of the claimed invention at the time the application was filed.

In view of the above remarks, Applicants respectfully request that the Examiner reconsider and remove the written description rejection under the first paragraph of 35 U.S.C. § 112.

Regarding the rejections under 35 U.S.C. § 102(a)

The rejection of claim 15 under 35 U.S.C. § 102(a), as allegedly anticipated by Zhang et al. Society for Neuroscience Abstracts (1999) is respectfully traversed. The Office Action states that Zhang et al. demonstrates that PrRP enhances nonREM sleep with febrile responses in rats.

Applicants respectfully submit that Zhang et al. does not teach the claimed invention. Specifically, whereas claim 15 is directed to a method for promoting sleep involving administering a PrRP receptor agonist, Zhang et al. describes the ability of PrRP to induce sleep. In particular, the reference states that at doses of 0.1 and 1 nmol, PrRP increased either REM sleep or both REM and nonREM sleep, respectively (sixth sentence). Zhang et al. further states that at high dose of 10 nmol, PrRP increased nonREM sleep (7^{th} sentence).

In contrast, the specification teaches that administration of 10 nmol PrRP to rats significantly decreased total time spent asleep, including slow wave sleep (nonREM sleep) and REM sleep, and accordingly increased total time spent awake (page 88, lines 18-30 and Figure 7 A-C). Further disclosed in the specification is that the conversion of PrRP treated animals to the awake state was nearly complete at a dose of 10 nmol and lasted for well over an hour (page 89, lines 6-8). Absent a teaching that a PrRP receptor agonist can promote wakefulness in a mammal, Zhang et al. cannot anticipate the invention.

In view of the above, Applicants respectfully request removal of the rejection of claim 15 under 35 U.S.C. § 102(a).

Regarding the rejection under 35 U.S.C. § 103

The rejections of claims 1, 13 and 14 under 35 U.S.C. § 103(a), as allegedly obvious over Zhang et al. in view of Curran et al. (U.S. Patent No. 6,323,177); and the

rejection of claims 2-10 under 35 U.S.C. § 103(a), as allegedly obvious over Zhang et al. in view of Curran et al. and further in view of Roland et al. Endocrinology 140:5736-5745 (1999), are respectfully traversed.

Applicants submit that the combination of Zhang et al. and Curran et al. does not teach or suggest the invention of claims 1, 13 and 14, but rather teaches away from the claimed invention. Specifically, whereas claim 1 is directed to identifying a PrRP receptor agonist for promoting wakefulness in a mammal, Zhang et al. describes experimental results indicating that PrRP promotes sleep (see, for example, the 6th and 7th sentences). Curran et al. does not cure the deficiencies of Zhang et al. in describing the claimed invention. Rather, this reference describes unrelated screening and therapeutic methods (column 1, lines 12-18).

Further, Applicants submit that the combination of Zhang et al. with Curran et al. provides no motivation for producing the claimed invention. In this regard, Zhang et al. states that administration of PrRP results in increased sleep at both low and high doses (0.1 and 10 nmol; 6th and 7th sentences). Based on these results, one skilled in the art would have had no motivation to screen PrRP receptor agonists to identify a compound for promoting wakefulness, but instead would have understood that a PrRP receptor agonist promotes sleep.

Regarding the rejection of claims 2-10, Applicants submit that the combination of Zhang et al. Curran et al. and

Roland et al. does not teach or suggest the invention of these claims. Whereas Zhang et al. indicates that administration of PrRP to rats resulted in increased sleep, the methods of claims 2-10 are directed to screening for a PrRP receptor agonist that promotes wakefulness. Neither Curran et al. alone or together with Roland et al. can cure the deficiencies in Zhang et al. in describing or suggesting the claimed invention.

In view of the above, Applicants submit that none of Zhang et al.; the combination of Zhang et al. with Curran et al.; or the combination of Zhang et al., Curran et al., and Roland et al., suggest or provide a motivation for producing the claimed invention. Therefore, Applicants respectively request that this ground of rejection be withdrawn.

CONCLUSION

In view of the amendments and the remarks submitted herein, Applicants submit that the claims are in condition for allowance and respectfully requests a notice to that effect. The Examiner is invited to contact the undersigned agent or Cathryn Campbell if there are any questions relating to this application.

Respectfully submitted,

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